

Document made available under the Patent Cooperation Treaty (PCT)

International application number: PCT/DK05/000036

International filing date: 21 January 2005 (21.01.2005)

Document type: Certified copy of priority document

Document details: Country/Office: DK
Number: PA 2004 00083
Filing date: 22 January 2004 (22.01.2004)

Date of receipt at the International Bureau: 11 February 2005 (11.02.2005)

Remark: Priority document submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b)



World Intellectual Property Organization (WIPO) - Geneva, Switzerland
Organisation Mondiale de la Propriété Intellectuelle (OMPI) - Genève, Suisse



Kongeriget Danmark

Patent application No.: PA 2004 00083
Date of filing: 22 January 2004
Applicant: SCF Technologies A/S
(Name and address) Ramsingsvej 30
DK-2500 Valby
Denmark

Title: Method and apparatus for producing micro emulsions

IPC: -

This is to certify that the attached documents are exact copies of the above mentioned patent application as originally filed.



Patent- og Varemærkestyrelsen
Økonomi- og Erhvervsministeriet

03 February 2005


Susanne Morsing

METHOD AND APPARATUS FOR PRODUCING MICRO EMULSIONS

FIELD OF INVENTION

5 This invention relates to preparation of micro emulsions having a controlled size. It provides methods, measures, apparatus and products produced by the methods. The method is particularly suitable for preparing micro emulsions of water containing one or more ionic species in an oil and/or dense fluid phase such as CO₂ containing fluids under near or supercritical conditions, thereby enabling the
10 use of said dense fluids as solvents for extraction of ionic species, nanoreactor templates and/or a carrier for further processing such as deposition on a solid material and/or in a process for producing fine particles, such as particles in the nano- or micrometer range.

15 BACKGROUND

Supercritical fluids exhibits particular attractive properties such as gas-like mass transfer properties such as diffusivity, viscosity and surface tension, yet having liquid-like properties such as solvation capability and density. Furthermore, the
20 solubility can be manipulated by simple means such as pressure and temperature. Thus, selective dissolution of certain groups of solutes in a supercritical fluid may be achieved by optimising density of the fluid phase. This tuneable solvation capability is an unique property that make supercritical fluids different from conventional liquids. Another major advantage of supercritical fluid extrac-
25 tion is rapid separation of solutes that can be easily achieved by reduction of pressure.

These attractive properties of such fluids at near or at supercritical conditions have attracted considerable attention for its potential applications as environ-
30 mentally friendly solvents for chemical processing. Many applications are under development in research laboratories all over the world. Examples include dry cleaning, impregnation (coating), extraction, reaction, synthesis of sub-micron particles, synthesis of advanced materials etc.

35 Carbon dioxide (CO₂) is the most widely fluid used for dense fluid applications because of its moderate critical constants (T_c = 31.1 °C, P_c 72.8 atm, and ρ_c = 0,47 g/cm³), non-toxic nature, low cost, and availability in pure form. Though

many CO₂ applications have been developed or are under development, high pressure CO₂ also exhibits some limitations. Since CO₂ is nonpolar and has weak Van der Waal forces, both polar and nonpolar non-volatile molecules often exhibit limited solubility or are virtually insoluble. For example, insoluble compounds such as electrolytes, biomolecules, polymers and inorganic compound
 5 can not be directly processed in high pressure CO₂.

The solubility of some of these classes of materials has been improved to some extent by applying co-solvents and/or surfactants in a mixture with CO₂ e.g.
 10 metals ions bound to organic ligands such as chelates becomes quite soluble in dense phase CO₂.

PARTICLE FORMATION

15 There are an increasing interest in nano- and micro-sized particulate materials in numerous technical applications. Such nanoparticulate materials exhibit properties, which are significantly different than those of the same material of larger size. Examples of physical properties, which decreases with decreasing particulate size are: Elastic modulus, density, thermal conductivity etc., whereas physical
 20 properties such as strengths, hardness, toughness, ductility, diffusivity, thermal expansion coefficient, solubility etc. increases as a result of size reduction of particulate materials. The novel properties of such nanostructured materials can be exploited and numerous new applications developed by using them in different industries. Examples of potential applications include new materials
 25 such as improved thermoelectrical materials, electronics, coatings, semiconductors, high temperature superconductors, optical fibres, optical barriers, photographic materials, organic crystals, magnetic materials, shape changing alloys, polymers, conducting polymers, ceramics, catalysts, electronics, paints, coatings, lubricants, pesticides, thin films, composite materials, foods, food additives,
 30 antimicrobials, sunscreens, solar cells, cosmetics, drug delivery systems for controlled release and targeting, etc.

Several techniques have been used in the past for the manufacture of micro- or nanoparticles. Conventional techniques include spray drying, freeze drying, milling
 35 and fluid grinding, which are capable of producing particles in the micrometer range. A particular high attention is related to techniques operating with solvent(s) at near or supercritical conditions, and in particular under supercritical

conditions. Several techniques for particle formation using supercritical fluids have been proposed over the last two decades. They are generally variations of two primary methods for particle precipitation in supercritical fluids, the Solvent-AntiSolvent technique (SAS) and the Rapid Expansion of Supercritical Solutions technique (RESS).

SAS Technique

In the SAS technique, the material of interest is first dissolved in a suitable organic solvent, and the solution is subsequently mixed with a supercritical solvent, which dissolves the solvent and precipitates the solids out as fine particles.

RESS Technique

In the RESS technique, the solid of interest is first solubilized in a supercritical fluid and thereafter expanded by spraying through a nozzle. The expansion through the nozzle causes a dramatic reduction in the CO₂ density and thereby a dramatic reduction in the solvent capacity, causing high supersaturation resulting in the formation of fine particles.

Derived techniques from the SAS and RESS techniques are for example Solution Enhanced Dispersion by Supercritical Fluids Techniques (SEDS) and Precipitation with compressed Antisolvent technique (PCA), which is based on the concept of coupling the use of a supercritical fluid as a dispersing agent, by means of a coaxial nozzle, in addition to its primary role as an antisolvent and a vehicle to extract the solvent. Further extensions of this technique includes multi concentric opening nozzles.

Other techniques includes Precipitation from Gas-Saturated Solutions (PGSS), which involves melting the material to be processed, and subsequently dissolving a supercritical fluid under pressure. The saturated solution is then expanded across a nozzle, where the supercritical fluid, which is more volatile escapes leaving dry fine particles.

All these techniques have been successfully used in small scale to produce micro-particles of various materials for numerous applications. Excellent reviews of prior art supercritical particle formation processes can be found in e.g. Ya-Ping

Sun("Supercritical Fluid Technology in Materials Science and Engineering - Syntheses, Properties and Applications, Marcel Dekker Inc., 2002-ISBN: 0-8247-0651-X), Gentile et al (WO03/035673A1), Gupta et al (US2002/0000681A1), Mazen et al (EP0706421B1), Del Re et al (WO02/068107A2), Mazen et al
 5 (WO99/44733), Calfors et al, Jagannathan et al (WO03/053561), all of which are hereby included by reference.

However, all these techniques suffer from some inherent limitations. The RESS technique is limited by the solvent capacity in the supercritical fluid. For exam-
 10 ple, supercritical carbon dioxide, which is a preferred solvent in many applica-
 tions, is limited by a low solubility of towards polar substances. Modifiers such as co-solvents and surfactants may be added to the supercritical carbon dioxide to improve the solubility of the material of interest. Drawbacks of the RESS tech-
 15 nique includes that the isenthalpic expansion over the nozzle that results in large
 temperature drops, which can cause freezing of the solid and carbon dioxide and thereby cause blocking of the nozzle. The nozzle design is further critical for the final particle characteristics such as size and morphology etc. All these draw-
 backs from microscopic variables limit the control over the process itself, and makes scale up difficult.

20

Due to the higher solubility the SAS technique and its derivatives generally have higher through puts, and generally produces particles in the range 1-10 micron (Gupta et al, US2002/0000681A1). The key and particle size controlling step of the SAS techniques is the mass transfer rate of the antisolvent into the droplet.
 25 Hence, mixing of solution and the supercritical fluid is crucial in order to obtain an intimate and rapid mixing, a dispersion of solution as small droplets into the supercritical fluid is required. Various nozzle designs have been proposed to in-
 ject solution and supercritical fluid into a particle formation vessel in order to provide a good mixing. Recent modifications of the SAS technique to reduce the
 30 particle size includes atomisation techniques such as special designed coaxial
 nozzles, vibrational atomisation, atomisation by high frequency sound waves, ultrasonic atomisation etc. (US20020000681A1). Though these modified tech-
 niques are believed to provide enhanced mass transfer and resulting reduced particle sizes, too rapid particle formation may reduce the control of the size and
 35 morphology such as crystallinity of the formed particles, be sensitive to the noz-
 zle design and blockages of the nozzle and be difficult to scale-up.

A more recent development and versatile method for production of fine particles involves the use of micellar structures as templates or nanoreactors. Micellar structures or emulsions are among the most frequently found colloidal systems, largely present in foods, cosmetics, pharmaceuticals, oils processing , paints etc.

- 5 They are colloidal dispersion of at least two immiscible liquids. The structure of the emulsions consists of droplets of a dispersed phase in a continuous phase. Typically such micelles are formed using surfactants to reduce the interfacial tension and stabilize the micelles. Such surfactants are amphiphilic molecules containing both a hydrophilic and a lipophilic segment. In normal micelles the
10 continuous phase is an aqueous and the lipophilic segment is arranged to interact with an organic phase. The opposite structures are called reverse micelles, and may be water-in-oil emulsions or water-in-CO₂ emulsions.

- Such reverse micelles and micro emulsions allow highly polar or polarizable
15 compounds to be dispersed in this nonpolar fluid. A wide range of nanomaterials can now be synthesized using ionic species or water soluble compounds as starting materials in the water cores of the micro emulsions. In these micro emulsion systems, the content of different micellar cavities undergo exchange when the micelles collide, creating opportunities for mixing and reactions be-
20 tween the reactants in the in the different cavities. Examples of applications of such systems are given in e.g. KP Johnson et al, "Water-in Carbon Dioxide micro emulsions: an environment of hydrophiles including proteins", Science: 271: 624-626, 1996, M. Ji et al: Synthesizing and dispersing silver nanoparticles in a water in super critical carbon dioxide micro emulsion, J. Am. Chem. Soc. 121:
25 2631-2632, 1999, H. Ohde et al: Synthesizing silver halide nanoparticles in supercritical carbon dioxide CO₂ utilizing a water-in-CO₂ micro emulsion), hereby included by reference. Other uses of such micro emulsions can be found in K.A. Barscherer et al, "Micro emulsions in compressible fluids – a review", Phase Equilibria 107:93-150, 1995. The water-in-CO₂ micro emulsions may also be
30 used as a medium for conducting electrochemistry in dense fluids (Ya-Ping Sun, Supercritical Fluid Technology in Materials Science and Engineering – Synthesis, Properties and Applications", Marcel Dekker, Inc., New York 2002, ISBN 0-8247-0651-X). Other applications include protein extraction, biocatalysis, dispersion polymerisation, emulsion polymerisation, metals extraction, dry cleaning, nano-
35 particle formation.

A number of advantages associated with the supercritical fluids-based emulsion

methods can be envisaged. For example the tuneable properties of supercritical fluids through pressure and/or temperature changes will provide more possibilities to manipulate the nanoparticles produced. For potential applications the preparation of nanoparticles in situ in a supercritical fluid system may be coupled
5 with other processes, such as rapid expansion for nanoscale coating and patterning. Another rationale for the use of supercritical fluid micro emulsion systems in the production of nanoscale materials is to take advantage of the templating effect associated with the rapid expansion technique (RESS, RESOLV). The supercritical fluid micro emulsions may be expanded e.g. into a liquid con-
10 taining a reactant for reaction with the reactant contained in the micro emulsion.

Since water and CO₂ are the two most abundant, inexpensive and environmentally compatible solvents, the application of such systems may have tremendous implications. Water-in-CO₂ and CO₂-in-Water micro emulsions under near or su-
15 percritical conditions have the ability to function as a universal solvent medium by solubilizing high concentrations of polar, ionic, and nonpolar nonvolatile compounds within the dispersed or continuous water phase.

However, though tremendous opportunities exist in applying such micro emul-
20 sions the practical embodiments for are still limited and rather inefficient. A wa-
ter- in- CO₂ emulsion is typically formed batch wise by adding water, proper surfactants, and electrolytes into a stirred pressure vessel, and compressing the vessel to the desired pressure by adding CO₂ and stirring the vessel in a time sufficient for the micro emulsions to form.

25 Such methods suffer from several drawbacks. First installing a stirrer in a high pressure vessel is relatively complicated and expensive. Secondly, they are generally limited to batch wise operation as the micro emulsions are formed from macro emulsions, which are cut into smaller emulsions until the desired size is
30 obtained. Though formation and breaking of micelles may be controlled to a certain extent by controlling the pressure and temperature, such methods re-
mains rather inefficient and methods improving the size control with a shorter processing time and having less energy consumption are highly desirable.

35 Hence, an objective of the present invention is to provide a continuous method and apparatus for producing micro emulsions of a controllable size.

Another objective of the present invention is to provide a methods and measures for improving the solubility of species, which exhibits a low solubility and/or are virtually insoluble in dense phase CO₂, so they can be dispersed and transported in dense phase CO₂.

5

Still Another objective of the present invention is to provide improved methods and measures for production of micro emulsions of more controllable size and uniform, e.g. micro emulsions of water in CO₂ or water in an organic solvent such as an oil.

10

A further objective of the present invention is to provide an improved method for the formation of fine particles with controlled growth rate, particle morphology and crystallinity and a narrow size distribution, which is less sensitive to drawbacks described in the prior art.

15

Still another objective of the present invention is to provide an improved method for producing nanoreactor templates more efficiently and with a more uniform size.

20 A further objective of the present invention is to provide a method and apparatus for producing a versatile solvent based on micro emulsions enclosed in compressed fluids, thereby enabling the use of said fluids for extraction of polar, ionic, and nonpolar nonvolatile species in high concentrations, and/or as a carrier for transporting dissolved or dispersed species for further processing such as
25 deposition on a solid matrix and/or for producing fine particles.

A still further objective of the present invention is to provide a method, which allows reduction of the surfactant concentration and/or the required density for stabilizing said micro emulsions.

30

An objective of the present invention is to provide a method, which allows mixing of more than one type of emulsion and allows easy and controllable addition or extraction of reactants in a continuous manner.

35

DESCRIPTION OF THE INVENTION

The present invention provides a novel way for production of micro emulsions in compressed fluids at near or at supercritical conditions, thereby enabling the use of said micro emulsion containing fluids as a versatile solvent for extraction of polar, ionic, and nonpolar nonvolatile species in high concentrations and/or as a carrier for transporting dissolved or dispersed species for further processing such as deposition on a solid matrix and/or for producing fine particles.

Hence, a preferred embodiment according to the present invention involves a method for producing emulsions in dense fluid(s) under near or supercritical conditions comprising

- Contacting the outer surface of a plurality of hollow tubular members with a first fluid, at least part of the walls of the hollow tubular members comprising membranes, the plurality of hollow fibres defining interstices therebetween allowing for flow of said first fluid, and
- Contacting a second fluid with the inner surface of said hollow tubular members, at least part of said second fluid is permeating said membrane walls forming a plurality of emulsion(s) of said second fluid dispersed in said first fluid.

In the present description with claims the term hollow tubular members comprises hollow fibres, and other hollow tubular bodies having any cross section, e.g. a hollow tubular chamber. Likewise the term the surface of a membrane and similar terms are intended to mean at least part of a membrane surface.

In one preferred embodiment according to the present invention, comprises a plurality of hollow fibre membranes. Typically the hollow tubular members is arranged into one or more section(s) or array(s) having a porous structure of any shape. Said one or more section(s) may further be arranged within a pressure housing such as a pressure vessel. Various ways of arranging such fibres are known in the prior art (e.g. W.S. Ho et al, "Membrane Handbook", Van Nordstrand Reinhold, 1992, ISBN 0-442-23747-2, K. Scott, "Handbook of Industrial Membranes", Elsevier Publicers, 1995, ISBN 1856172333, Iversen et al, WO95351153, Iversen et al, WO00160095, US690,830, US5,690,823) and are

hereby included by reference. Such methods includes random packings, mats, cloths, bundles, twisted bundles, meshes, arrays etc.

The inner surface of said hollow tubular members generally have one end communicating with an inlet plenum for feeding said second fluid to the lumen side (inner surface) of said hollow tubular members, and the other end of said tubular members communicating with an outlet plenum for collection the remaining part of said second fluid after passage through the lumen of said hollow tubular members. Likewise, the pressure housing will generally comprise one or more inlets for introducing said first fluid and/or surfactants and one or more outlets for withdrawing said first fluid containing said emulsions formed.

In an aspect the present invention comprises a plurality of fibres extending in substantially the same direction. One way of packing such fibres relevant to the present invention is disclosed in US 5,690,823 hereby included by reference.

In many embodiment according to the present invention the membrane is porous, and have pores in the range 0,001-100 micron, such as pores in the range 0,001-10 micron and preferably in the range 0,01-0,2 micron.

The hollow tubular member material may comprise a wide range of materials depending on the specific application. Nonlimiting examples of materials suitable for the present invention includes polymers from polypropylene, polyethylene, polystyrene, polyether polymers, polyamide, polyacrylic, polyimide, fluoropolymers, ceramics, and elastomers such as natural, synthetic and cured rubbers, and silicones (siloxane polymers).

An important embodiment of the present invention involves the production of micro emulsions in dense fluid(s) under near or supercritical conditions. A particular important fluid in this relation is compressed CO₂ such as liquid CO₂ near the critical point or supercritical CO₂. Another important fluid is water and/or a water mixture containing one or more substances being dissolved or dispersed therein. Said substances may be substantially insoluble in the compressed CO₂ and may e.g. comprise polar molecules and/or polarizable molecules and/or non-polar non-volatile molecules. Other important fluid(s) in relation to the present invention are organic solvents such as an oil.

The compressed CO₂ fluid phase contacting the outer surface of said hollow tubular members may further comprise one or more co-solvent(s). Suitable co-solvents includes alcohols, water, ethane, ethylene, propane, butane, sulfurhexafluoride, nitrous oxide, chlorotrifluoromethane, monofluoromethane, methanol, ethanol, DMSO, isopropanol, acetone, THF, acetic acid, ethyleneglycol, polyethyleneglycol, n,n-dimethylaniline etc., and mixtures thereof.

The compressed CO₂ fluid will generally also comprise one or more surfactant to stabilise said micro emulsions formed. Suitable surfactants comprises a CO₂-philic and a CO₂-phobic segment and includes chelates, fluorinated surfactants, perfluoroether surfactants, perfluoropolyether surfactants, fluoroetherfluoroacrylate and siloxane surfactants. Particular suitable surfactants may be selected from the group of hydrocarbons and fluorocarbons having a hydrophilic/lipophilic balance value (HLB) of less than 15, where the HLB value is determined according to the following formula:

$$\text{HLB} = 7 + \text{sum}(\text{hydrophilic group numbers}) - \text{sum}(\text{lipophilic group numbers}).$$

20

DESCRIPTION OF THE DRAWINGS

Fig. 1. shows a hollow tubular member containing device comprising a plurality of hollow tubular members extending in substantially the same direction and communicating with both an inlet and an outlet plenum. The lumen side (internal surface) of said plurality of hollow tubular members are sealed from the shell side (outer surface) by "potting" the hollow tubular members in both ends using a potting material. The potting of hollow tubular members can be carried out in any suitable manner and such procedures are well known in the art (e.g. US 3,422,008, US3,339,341, US 3,442,389, US 3,455,460, US 3,690,465, US 4,207,192, US 5,264,171, EP 0562520A1 etc.), all of which are incorporated by reference. The potting material can be organic or inorganic or a mixture thereof. Suitable potting materials are well known and described in US 4,369,605 and US 3,422,008 incorporated herein by reference. The plurality of hollow tubular members are arranged in a pressure housing as shown in the figure 1a. The first fluid and surfactant(s) is typically introduced through an inlet port on the shell side of the hollow tubular members, and contacts the outer surface of said hol-

low tubular members during the passage between the interstices between the hollow tubular members in said hollow tubular member array as shown in the drawing. The second fluid is introduced into said inlet plenum and is distributed to the lumen side (inner surface) of said tubular member(s). At least part of said
 5 fluid permeating through the membrane walls of said tubular members so as to obtain a controlled addition of said second fluid and/or dissolved substances to said first fluid on the outer surface of said hollow tubular members. The hydrophilic part of the surfactant(s) combines with the nanosized droplets of said second fluid formed at the outer surface of said membrane part of said hollow tu-
 10 bular members as illustrated in figure 1c-1d, and the micro emulsions of said second fluid optionally containing substances dissolved and/or dispersed therein. The micro emulsions formed may be continuously withdrawn from the hollow tubular member containing devices as indicated.

15 Fig. 2 shows an example of superimposed layers of hollow tubular members, where two different fluids (A and B) can be conducted through the lumen of the fibres, as indicated, whereas a flow of a third fluid can be passed transversely through the fibres from above, perpendicular to the longitudinal direction of the fibres, as indicated by the vertical arrow.

20

Fig.3 illustrates a situation similar to the one in Fig. 2, but where a woven array of hollow membrane fibres is used.

Fig.4 shows an example of an array of hollow tubular members, wherein the
 25 hollow tubular members are constituted by elongated chambers arranged longitudinally substantially parallel to each other, the longitudinal surfaces of the chambers having at least one region, being constituted by at least one membrane. The horizontal arrow indicates the direction in which the first fluid moves and the two vertical arrows indicates the direction in which the second fluid
 30 moves. The membrane surfaces are not explicitly shown in the figure, but one or more membrane surface(s) is/are preferably arranged on each of the sides parallel to the direction in which the first fluid moves. The enlarged section shows the chambers in which the first fluid moves. The enlarged section shows the chambers and the outlet plenum. In order to obtain a rigid array of cham-
 35 bers, especially where a large part of the individual chamber surface is constituted by a flexible flat membrane, the individual chambers or adjacent chambers may be supported by a supplementary structure. Thus in a preferred embodi-

ment the chambers comprise a perforated-, porous, mesh- or netstructure. The array of hollow tubular members is generally arranged in a pressure housing. This pressure housing may e.g. be part of a tubing or conduit for carrying said first fluid as illustrated in the drawing. It should be noticed that a multiplicity of
 5 such arrays may be superimposed in the direction of said first fluid and arranged in the same pressure housing. It should further be noticed that the hollow tubular member array(s) may have other kinds of cross section or be a segment of a cylindrical conduit such as described in WO9535153.

10 Fig. 5 shows an example of two hollow tubular member containing devices, wherein two different micro emulsions of said second fluid containing at least two different electrolytes dissolved therein is formed in two different streams of said first fluid containing two different surfactants. The two streams containing
 15 said micro emulsions are mixed and reacted in a third device e.g. a pressure vessel. An important embodiment according to the present invention is where said pressure vessel further comprising a solid matrix for deposition of said materials formed from reaction between said electrolytes contained in said micro emulsions formed. After a certain treatment time within said pressure vessel, the materials formed are deposited on the surface of said solid matrix by break-
 20 ing the emulsions by decreasing the density of said first fluid by a change in the pressure and/or the temperature of said first fluid or by a combination thereof. Nonlimiting examples of where this invention may be applied is the in production heterogeneous catalysts, various kinds of ceramics e.g. ceramic membranes, fuel cells, solar cells, electronics, semiconductors, magnetic materials, thermoe-
 25 lectrical materials, photographic materials, conducting polymers, medical articles etc. wherein a thin layer of a nanoparticulate material is desired.

ILLUSTRATIVE EXAMPLE 1

- 30 In an aspect of the present invention a micro emulsion of water-in-CO₂ is continuously formed by introducing
- a compressed CO₂ stream to the inlet plenum for the first fluid and thereby contacting the outer surface of a plurality of hollow tubular members with
 35 said first fluid.
 - one or more surfactant(s) to the first fluid either by premixing the compressed CO₂ stream with the surfactant, or introducing the surfactant to the

same inlet plenum as for said first fluid, or through a separate inlet point, and thereby contacting said outer surface of said plurality of hollow tubular members with a compressed CO₂ fluid containing said surfactant(s).

- a compressed water stream to the inlet plenum for the second fluid and
- 5 thereby contacting said second fluid with the inner surface of said plurality of hollow tubular members.

Part of the water phase contacting said inner surface of said hollow tubular members permeates through the membrane part of said hollow tubular mem-
10 bers, and thereby a nano- or microatomization occurs, and thereby resulting in very small droplets being formed at the outer surface of said hollow tubular members, and thereby resulting in the formation of micro emulsions of water-in-CO₂ at the outer surface.

- 15 The membrane characteristics have an impact of diameter of the water core in the emulsions formed, and in general the diameter of the water core is in the range 0,001-30 times the diameter of membrane pores at the outer surface, and is preferably in the range 0,01-15 times the diameter of membrane pores at the outer surface.

20

The amount and size of the emulsions may further be controlled by controlling the pressure, temperature and flow rate of both the fluids as well as by controlling surfactant concentration.

- 25 In general the flux of water through the membrane is controlled by maintaining a higher pressure of the second fluid than of the first fluid, thereby creating a pressure differential over said membrane. According to the present invention the pressure differential is generally maintained in the range 0,01-100 bars, and preferably in the range 0,1-30 bars depending on the specific application.

30

The pressure and temperature of the first fluid depends on the specific application. In general the pressure of the first fluid is maintained in the range 50-500 bars, preferably in the range 85-500 bars, such as in the range 100-300 bars. The temperature within the vessel is generally maintained within the range 20-
35 500 °C, such as in the range 30-450 °C, and preferably in the range 35-150 °C, such as in the range 40-100 °C.

The compressed CO₂-phase containing said micro emulsions formed may be continuously withdrawn from the outlet plenum for said first fluid, and is suitable as a versatile solvent for extraction of polar, ionic and/or nonpolar nonvolatile species in a device external to the micro emulsion producing device.

5

Nonlimiting examples of applications for use of said solvent includes extraction or dissolution of proteins, metals etc., and processes for cleaning of textiles, metal and semiconductor parts etc.

10 ILLUSTRATIVE EXAMPLE 2

The hollow tubular member containing device described in illustrative example 1, generally constitute a large contact area between said first fluid and said second fluid.

15

In many applications according to the present invention this large contact area between the fluids is used to control the temperature within the hollow tubular member containing device.

20 This is generally performed by controlling the flow rate and inlet temperature of said second fluid, and withdrawing the remaining part from said outlet plenum for said second fluid to a an external re-circulation loop, wherein heat is added and/or extracted in the re-circulation loop and feeding the fluid back to the inlet plenum for said second fluid.

25

Hereby the temperature of both the first and the second fluid can be accurately controlled within the hollow tubular member containing device.

ILLUSTRATIVE EXAMPLE 3

30

Many applications according to the present invention involves the continuous production of micro emulsions of water in CO₂, wherein the water core of said micro emulsions contains dissolved and/or dispersed substances such as electrolytes dissolved and/or dispersed therein.

35

In such applications the compressed water stream described in the illustrative examples 1 and 2 will generally contain such dissolved and/or dispersed species

in a predefined concentration, and the membrane characteristics and pressure differential over said membrane will be adapted to control the concentration of said species in the micro emulsions formed in a predefined manner.

- 5 The compressed CO₂-stream containing said micro emulsions with dissolved and/or dispersed substances therein, may be continuously withdrawn from the outlet plenum for said first fluid.

- In a preferred embodiment said compressed CO₂-stream is used as a carrier for
- 10 transporting said dissolved and/or dispersed species into an external device, e.g. a coating or impregnation vessel containing a solid material to be coated with said dissolved and/or dispersed species. After a certain treatment time said dissolved and/or dispersed species is deposited on the surface of said solid material, by decreasing the density of said compressed CO₂ stream. This decrease in
- 15 density is generally performed by reducing the pressure and/or the temperature in the vessel containing said solid material or by a combination thereof.

- Nonlimiting examples of coating applications for use of said compressed CO₂ stream containing micro emulsions with substances dissolved or dispersed
- 20 therein includes deposition of metal compounds in production of electronics, catalysts, medical devices, polymers such as conducting polymers etc.

ILLUSTRATIVE EXAMPLE 4

- 25 Many biological and pharmaceutical materials are hydrophilic as they derive from living cells and are readily soluble in water and virtually insoluble in organic solvents and also possess a low solubility in dense phase CO₂. Examples of such classes of compounds include proteins, peptides, nucleic acids and pharmaceutical excipients such as carbohydrates and sugars, fillers and biologicals. Dissolu-
- 30 tion of such materials in organic solvents and/or exposure to heat and/or air often cause denaturation of such materials, thereby reducing the bioactivity of such materials.

- The crystallinity is another very important issue in the pharmaceutical industry
- 35 not only affecting drug stability but also affecting its dissolution rate. An amorphous form shows faster dissolution than the crystalline form of a given material. It is therefore desirable to control the crystallinity during material process-

ing. Small amounts of water may increase the crystallinity (desirable in many applications).

Processing of such classes of compounds are important in relation to the present invention. Such materials may be processed in the same way as described in the previous examples. The material(s) in question may be dissolved or dispersed a compressed aqueous stream, and atomized through said membrane(s) to form micro emulsions of water-in-CO₂.

10 Suitable surfactants for use in such systems may include a hydrophilic sugar group and a double tail of CO₂-philic molecules such as PDMS, fluoroalkyls, fluoroethers or others.

The compressed CO₂ stream containing said micro emulsions formed may be used as a carrier to transport said micro emulsions to an external device, e.g. a vessel containing a solid material for deposition of said dissolved species or to a particle formation device. An example of an application, wherein a deposition is involved is the production of biocatalyst by deposition of enzymes on a polymeric matrix. Another important embodiment is the use micro emulsions formed in processes for production of fine particles such as particles in the nano- or micrometer range as further exemplified below.

ILLUSTRATIVE EXAMPLE 5

25 In one embodiment according to the present invention two or more emulsions are formed in the same hollow tubular member containing device by applying two or more separate sets of hollow fibres. All sets of hollow fibres comprising an inlet and an outlet plenum communicating with the outside of said hollow tubular member containing device, and wherein two or more separate fluids may be contacted with the inner surface of said hollow tubular members, thereby producing two or more different emulsions of said fluids in the first fluid contacting the outer surface of said hollow tubular members.

In an alternative embodiment production of two or more emulsions containing different dissolved species is performed in separate hollow tubular member containing devices, and the first fluid of said devices combined in an external device, as illustrated in figure 5.

Upon combination of the micro-emulsion fluids in the external device, intermicellar contact or combination of micelles containing different solutes leads to chemical reactions in the micelle cavities. The second fluids of the hollow tubular member containing devices, forming the emulsions, should be compatible, and preferably the same fluids, so as to allow contact between the emulsions.

Combination of, or contact between, the different emulsions produced in separate hollow tubular member containing devices, and containing the dissolved reactants, may be enhanced by designing the surfactants used in the emulsion formation to facilitate contact between micelles of different content. The facilitation of contact between micelles of different content may be achieved by an electrostatic force, induced by including a molecular charge displacement in the lipophilic part of the surfactant, and thereby creating a polarity in the molecule, with an electrically charged part of the molecule facing the continuous phase, i.e. the bulk of the first fluid. The electrical charge will cause attraction of surfactants with opposite charge, and repulsion of surfactants with identical charge. Introducing such polarity of opposite charges in the lipophilic part of the surfactants used to produce two micro-emulsions will facilitate contact between micelles containing different solutes, while reducing merging of micelles of the same solute content. Nonlimiting examples of organic molecular groups introducing polarity are halogenated alkyls or aryls, aldehydes, ketones, ethers, hetero-cyclic structures containing oxygen, nitrogen or sulphur, amines, amides or mercaptanes.

In both cases the exchange between the different micellar cavities may be enhanced by applying a pulsation effect, and/or an ultrasound effect and/or an vibrating surface effect in the device, wherein said exchange between different micellar cavities occurs. The pulsation effect may be performed by modulating the density of said first fluid containing said emulsions between an uppermost and a lowermost level. This density modulation may be performed by modulating the pressure and/or the temperature. Typically the density change between the uppermost and lowermost density level is up to 75 %, such as up to 50 %, and preferable up to 30 % and the density modulation may be repeated multiple times such as 5-100 times.

ILLUSTRATIVE EXAMPLE 6

An important micro emulsion system according to the present invention, as described in example 5, is the use of the micro emulsions as templates for the syntheses of particles. Many of such systems involves intermicellar exchange of different dissolved and/or dispersed substances, when the micelles collides and thereby facilitates mixing, and subsequent reactions, between the reactants contained in the different micellar cavities. An example of such system is a reverse micelle containing a metal salt dissolved in the water core and sulfide ions in the water core of another micelle. Intermicellar exchange results in the formation of metal sulfide nanoparticles within the nanoscale reverse micelle cavities. Particle growth stops due to the limitation of the particle size that the micelle can support, and the particle size may to a certain extent be controlled by changing the CO₂ solvent properties.

The particle formation due to exchange between the different micellar cavities may take place as a batch process within said hollow tubular containing device, or the first fluid containing said mixed micelles may be continuously withdrawn to an external device as described in illustrative example 1.

In another preferred embodiment only one compressed water stream containing metal containing substances dissolved or dispersed therein, is fed to the inlet plenum of one set of hollow tubular members, at least part of the compressed water stream permeating the membrane part of said hollow tubular members and forms micro emulsions in said first fluid contacting the outer surface of said hollow tubular members, while a third fluid containing a reducing agent such as an alcohol, hydrazine, hydrides, alkalides, Grignard reagents etc. is continuously fed to the second set of hollow fibres, and where a controlled addition is obtained by control of the flow rate and/or pressure of said third fluid. Contact between micelles containing the metal and the reducing agent leads to formation of metal nano-particles. The formed metal nanoparticles are harvested by expansion of the first fluid, and collection in conventional devices for particle collection, or might be deposited directly on a substrate, as a surface treatment of said substrate to form the final product.

35

ILLUSTRATIVE EXAMPLE 7

The emulsion formation techniques described in any of the previous examples may suitably be combined with any of the prior art particle formation processes using dense phase fluids, e.g. RESS (rapid expansion of supercritical solution),
5 RESOLV (rapid expansion into a liquid solvent), SAS (solvent anti solvent), SEDS (solution enhanced dispersion by supercritical fluid), PCA (precipitation with compressed antisolvent) and variations thereof.

10 ILLUSTRATIVE EXAMPLE 8

A preferred embodiment according to the present invention is the formation of fine particles with subsequent deposition in a thin layer on a solid material comprising the end product. Nonlimiting examples of such applications is ceramic
15 membranes, fuel cells, solar cells, semiconductors, self cleaning mirrors, conducting polymers, catalysts etc.

Another class of applications applicable to a method according to the present invention is within life sciences, e.g. deposition of one or more drugs and/or bio-
20 molecules on the surface of a polymer matrix, so as to obtain new functionalities such as controlled release, targeted release etc. in medical and/or pharmaceutical articles.

Still another class of applications applicable to a method according to the present invention, is the deposition of antimicrobial compounds on the surface of polymers used as medical articles used in relation to surgeries and/or as in-body devices such as implants.
25

An additional advantage of the present invention in relation to the latter two applications is that the processing may be performed under sterile conditions as
30 high pressure CO₂ in itself exhibits sterilisation properties, and the final product may be processed so as to maintain a positive pressure of CO₂ within the article until packaging, thereby minimising the risk of cross contamination. By maintaining a positive pressure of CO₂ within the article produced until packaging the
35 article will also be maintained within an inert atmosphere after packaging.

ILLUSTRATIVE EXAMPLE 9

There are several reasons for employing drugs as fine powders in pharmaceuticals, such as the need to improve the bioavailability of the drug or the requirement for specific pharmaceutical forms (nasal, ophthalmic, injectables, modified release etc.).

As described in illustrative example 4, one of main the problems related to processing of biomolecules such as peptides and proteins e.g. enzymes etc., is that they easily loose bioactivity in contact with the organic solvent typically employed for supercritical processing of such biomolecules due to denaturation of the steric composition and they may further change crystallinity in the absence of water.

A new supercritical emulsion drying technique for preparation of inhalable protein particles was disclosed by J.Jung et al. at the 6th International Symposium on Supercritical Fluids in Versailles (France), April 28.-30., 2003 (J. Jung, F. Leboeuf, and M. Perrut, "Preparation of inhable protein particles by SCF Emulsion Drying", In Proc. of 6th International Symposium on Supercritical Fluids, Tome 3: Materials Processing, p.1837-1842, 2003, ISBN 2-905-267-37-02, and M. Perrut et al, FR0106403), hereby included herein by reference.

In this technique, water-in-oil emulsion droplets containing dissolved proteins such as trypsin, catalase, lactase and insuline etc. was sprayed into a continuous feed of high pressure carbon dioxide. Protein particles precipitated as micron sized particles as a result of expansion of the droplets and removal of water by the CO₂ organic solvent mixture. The micron size particles showed a significantly higher preservation of bioactivity than for usual supercritical processing.

The method according to the present invention is suitable for continuous production of such water-in-oil emulsions containing dissolved and/or dispersed substances from a wide range of materials. Said micro emulsions may be further processed according to any supercritical method such as the one described above or in illustrative example 7.

CLAIMS

1. A method of producing emulsions in dense fluid(s) under near or supercritical conditions comprising
 - 5 - Contacting the outer surface of a plurality of hollow tubular members with a first fluid, at least part of the walls of the hollow tubular members comprising membranes, the plurality of hollow fibres defining interstices therebetween allowing for flow of said first fluid, and
 - 10 - Contacting a second fluid with the inner surface of said hollow tubular members, at least part of said second fluid is permeating said membrane walls forming a plurality of emulsion(s) of said second fluid dispersed in said first fluid.
- 15 2. A method according to claim 1, wherein one of the fluids is compressed CO₂.
3. A method according to claim 2, wherein the compressed CO₂ is a compressed liquid.
- 20 4. A method according to claim 2, wherein the compressed CO₂ is a supercritical fluid.
- 25 5. A method according to any of the preceding claims, wherein one of the fluids is water or contains water.
6. A method according to claim 5, wherein said water or water mixture further contains one or more substances preferably being dissolved and/or dispersed therein.
- 30 7. A method according to any of the claims 5-6, wherein said one or more substances comprises polar molecules and/or polarizable molecules and/or non-polar, non-volatile molecules.
- 35 8. A method according to claim 7, wherein said one or more substances is substantially insoluble in compressed CO₂.

9. A method according to any of the preceding claims, wherein one of the fluids is an organic solvent, such as an oil.
- 5 10. A method according to any of the preceding claims, wherein said CO₂ containing fluid further comprises at least one co-solvent.
- 10 11. A method according to claim 10, wherein the co-solvent is selected from the group consisting of alcohol, water, ethane, ethylene, propane, butane, sulfurhexafluoride, nitrous oxide, chlorotrifluoromethane, monofluoromethane, methanol, ethanol, DMSO, isopropanol, acetone, THF, acetic acid, ethyleneglycol, polyethyleneglycol, N,N-dimethylaniline etc. and mixtures thereof.
- 15 12. A method according to any of the preceding claims, wherein said CO₂ containing fluid further comprises one or more surfactants, comprising a CO₂-philic portion and a CO₂-phobic portion.
- 20 13. A method according to claim 12, wherein said surfactant(s) is/are chelate(s) and/or fluorinated surfactants, and/or perfluoropolyether surfactants, and/or fluoroetherfluoracrylate surfactants and/or siloxane surfactant(s).
- 25 14. A method according to any of the claims 12-13, wherein said surfactant(s) being selected from the group consisting of hydrocarbons and fluorocarbons preferably having a hydrophilic/lipophilic balance value of less than 15, where the HLB value is determined according to the following formula: $HLB = 7 + \text{sum}(\text{hydrophilic group numbers}) - \text{sum}(\text{lipophilic group numbers})$.
- 30 15. A method according to any of the preceding claims, wherein the molar ratio of compressed surfactant to the dissolved and/or dispersed molecules in said second fluid is at the most 100:1, such as at the most 50:1, and preferably at the most 30:1 such as at the most 10:1.
- 35 16. A method according to any of the preceding claims, wherein the pressure of at least one of said fluids is in the range 50-500 bars, preferably in the range 85-500 bars, such as in the range 100-300 bars.

17. A method according to any of the preceding claims, wherein the temperature in said hollow tubular member containing device is maintained in the range 20-500 °C, such as 30-450 °C, and preferable in the range 35-200 °C, and more preferable in the range 40-150 °C.
- 5 18. A method according to any of the preceding claims, wherein said emulsion formed is a micro- or nano emulsion.
19. A method according to claim 18, wherein said micro emulsion formed comprises a water core.
- 10 20. A method according to claim 19, wherein said water core comprises dissolved and/or dispersed substances.
- 15 21. A method according to any of the claims 18-20, wherein the diameter of said water core in the emulsions formed is in the range 0.001-30 times the diameter of the pores of the membrane part of said hollow tubular members, such as in the range 0.01-15 times the diameter of the pores of the membrane part of said hollow tubular members, and preferably in the range
- 20 0.1-10 times the diameter of the pores of said hollow tubular members.
22. A method according to any of the preceding claims, wherein the pressure of the fluid(s) contacting the inner surface of said hollow tubular members is higher than the pressure of the first fluid.
- 25 23. A method according to claim 22, wherein the pressure differences between the fluid(s) contacting the inner surface of said hollow tubular members and the first fluid is in the range 0,01-100 bars, such as in the range 0,1-50 bars, and preferably in the range 0,1-20 bars such as in the range 0,1-10
- 30 bars.
24. A method according to any of the preceding claims, wherein the membrane part of said hollow tubular members comprises porous membranes
- 35 25. A method according to claim 24, wherein the pore size of said porous membranes is in the range 0,001-100 microns, such a pore size in the range 0,01-10 micron, and preferably having pores in the range 0,01-0,2 micron.

26. A method according to any of the preceding claims, wherein said hollow tubular members are hollow fibres.
- 5 27. A method according to any of the preceding claims, wherein the membrane is a ceramic or polymeric membrane.
- 10 28. A method according to any of the preceding claims, wherein said tubular members comprises two separate set of hollow tubular members, both sets of said hollow tubular members comprising an inlet and an outlet plenum communicating with the outside of said hollow tubular member containing device, and wherein two separate fluids may be contacted with the inner surface of said hollow tubular members, and wherein two different emulsions of said fluids in said first fluid contacting the outer surface of said
15 hollow tubular members are formed.
- 20 29. A method according to claim 28, wherein said two different emulsions is produced in separate hollow tubular member containing devices, and the first fluid of said devices is combined in an external device.
30. A method according to any of the claims 28-29, wherein said two different emulsions are formed using at least two different surfactants
- 25 31. A method according to claim 30, wherein said surfactants are designed with electrostatic forces so as to facilitate contact of micelles of different type and reduce merging of micelles of same type.
- 30 32. A method according to claim 31, wherein said electrostatic force are induced by including a molecular charge displacement in the lipophilic part of the surfactant.
- 35 33. A method according to claim 32, wherein said molecular charge displacement are obtained by introducing polarity from organic molecular groups selected from halogenated alkyls and/or aryls, and/or aldehydes, and/or ketones, and/or ethers, and/or hetero-cyclic structures containing oxygen, nitrogen and/or sulphur and/or amines and/or amides and/or mercaptanes

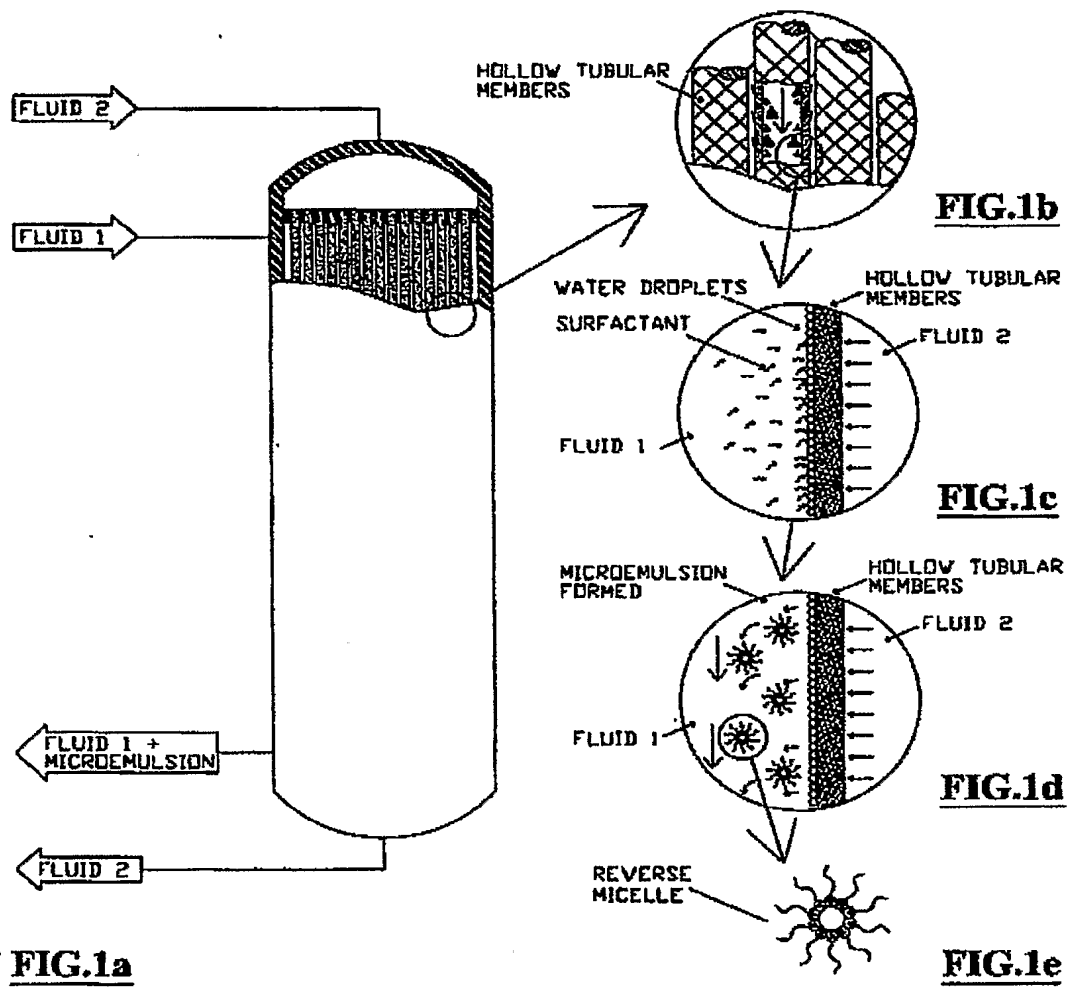
34. A method according to any of the preceding claims, wherein said micro emulsion(s) is/are used as nanoreactors for synthesis of nanoparticle materials.
- 5 35. A method according to claim 34, wherein said micro emulsions is used as a template for controlling said particulate material into a specific shape, size and/or structure.
- 10 36. A method according to any of the preceding claims, wherein size of said nanoparticle material formed is in the range 0-5000 nm, such as 0-500nm, preferably in the range 0-100 nm, and most preferable in the range 0-30 nm, such as 0-15 nm.
- 15 37. A method according to any of the preceding claims, wherein a chemical reaction is occurring in said micro emulsions.
38. A method according to the claims 34-37, wherein said synthesis of said nanomaterials is controlled by controlling temperature and/or pressure.
- 20 39. A method according to any of the preceding claims, wherein the first fluid containing said micro emulsion(s) is/are expanded.
40. A method according to claim 39, wherein the first fluid is rapidly expanded using a RESS or a RESOLV technique.
- 25 41. A method according to any of the preceding claims, comprising re-circulating in at least part time of the method at least part of a fluid or fluid mixture present in the hollow tubular member containing device, the re-circulating comprising:
- 30 withdrawing from the vessel at least a part of a fluid from said hollow tubular member containing device and feeding it to a re-circulation loop and subsequently feeding the fluid back to the hollow tubular member containing device.
- 35 42. A method according to claim 41, further comprising the step of controlling the temperature of the fluid in the re-circulation loop.

43. A method according to any of the preceding claims, wherein the temperature profile within said hollow tubular member containing device(s) is controlled by controlling the temperature and flow rate of at least one fluid contacting the inner surface of said hollow tubular members.
44. A method according to any of the preceding claims, wherein said hollow tubular member containing device(s) is operating continuously at a substantially constant pressure.
45. A method according to claim 44, wherein said first fluid containing said micro emulsion(s) formed is continuously withdrawn from said hollow tubular member containing device.
46. A method according to claim 45, wherein said first fluid containing said micro emulsion(s) formed is used to dissolve and/or extract substances outside said hollow tubular member containing device.
47. A method according to any of the claims 44-46, wherein said first fluid containing said micro emulsions is/are used as a carrier(s) for transporting dissolved and/or dispersed species to an external device.
48. A method according to claim 47, wherein the content of said micro emulsions formed is/are deposited on the surface of a solid material.
49. A method according to claim 48, wherein said treated solid material comprises a medical and/or a pharmaceutical article.
50. A method according to any of the claim 48-49, wherein the deposited material constitutes a layer of primary particles having a diameter of the most 30 nm such as at the most 20 nm, such as at the most 10 nm.
51. A method according to claim 50, wherein the thickness of said layer is at the most 500 nm, such as at the most 100 nm, and preferably at the most 50 nm such as at the most 25 nm.
52. A method according to claim 47, wherein said external device is an appa-

ratus for producing fine particles.

53. A method according to claim 52, wherein one or more additional fluids containing substances dissolved and/or dispersed therein, is introduced in
5 to said external device, so as to perform a micro encapsulation of said fine particles formed.
54. A method according to claim 52, wherein said external device contains a solvent and said fine particles are collected as a dispersion of said fine particles within said solvent.
10
55. A method according to claim 52, wherein said solvent further comprises a reactant for said particle formation process.
- 15 56. A method according to any of the preceding claims, wherein said primary particles formed comprise one or more pharmaceutical and/or biological material.
57. A method according to any of the preceding claims, wherein said material being deposited and/or collected comprises a metal or a semi-metal or a combination thereof.
20
58. A method according to any of the claims 57, wherein the electrolyte dissolved and/or dispersed within said micro emulsions is/are a reactant(s) in
25 a supercritical sol-gel reaction.
59. A method according to any of the preceding claims, wherein said fine particles formed comprises oxide(s) such as metal oxide(s) or semi-metal oxide(s).
30
60. A method according to claim 59, wherein said oxides is a thermoelectrical material or a precursor for production of a thermoelectrical material.
- 35 61. A method according to claim 60, wherein said thermoelectrical material or precursor for said thermoelectrical material comprises Bi_2Te_3 or Bi_2Te_3 doped with semimetals and/or metals.

62. A method according to any of the claims 57-59, wherein said oxide(s) are an oxygen ion conducting oxide(s) such as $\text{Ce}_{1-x}\text{Gd}_x\text{O}_{2-x/2}$, LaGaO_3 , or doped ZrO_2
- 5 63. A method according to any of the claims 57-58 , wherein said primary particles formed are carbide(s) and/or nitride(s) and/or sulfides and/or borides and/or hydrides.
- 10 64. An apparatus comprising means according to any preceding claims thereby being adapted to carry out the method according to any of the preceding claims.
65. A process comprising steps according to a method of any of the preceding claims.
- 15 66. A product produced from a method according to any of the preceding claims.



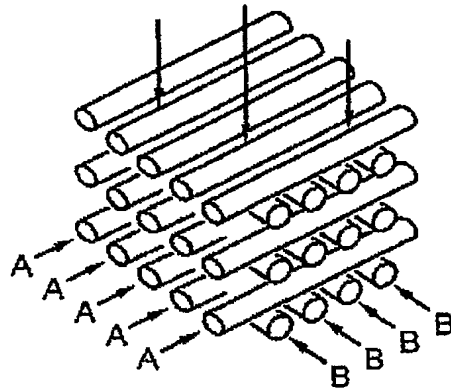


FIG. 2

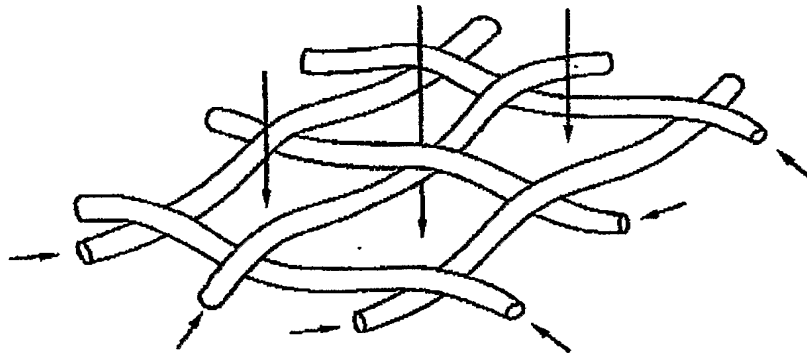


FIG. 3

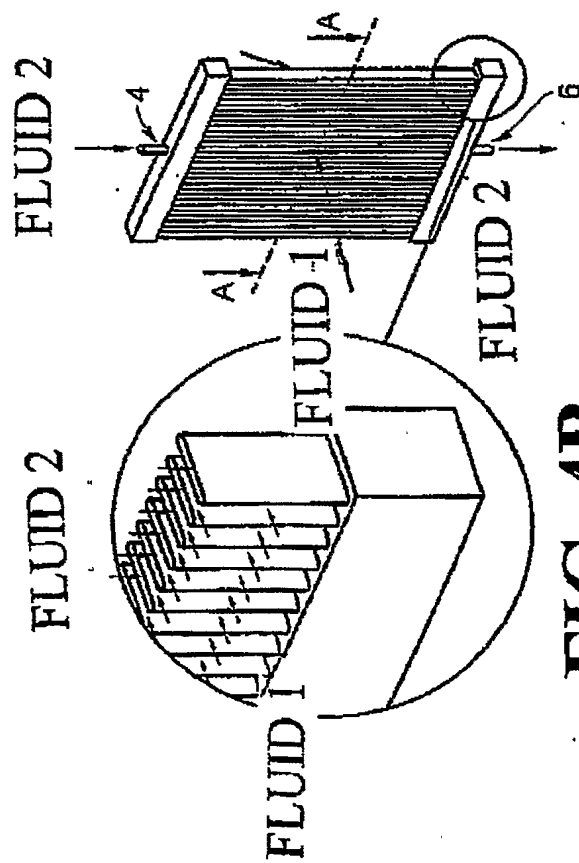


FIG. 4B

FIG. 4A

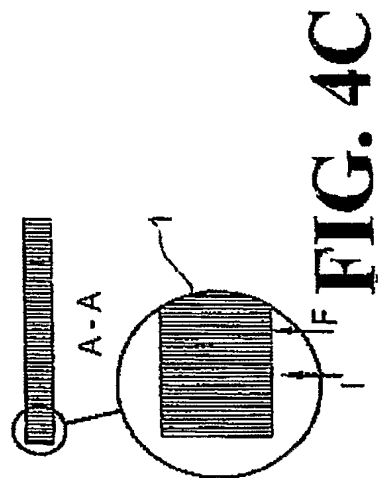


FIG. 4C

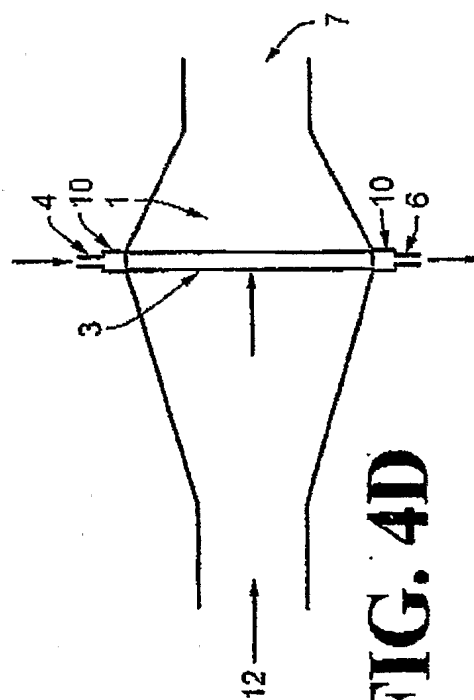


FIG. 4D

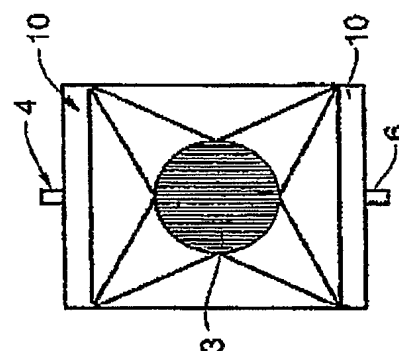


FIG. 4E

FIG.5

